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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/547,220	04/11/2000	Michael Brines	10165-006-999	4714

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PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	13

DATE MAILED: 05/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/547,220	Applicant(s) BRINES ET AL.	
	Examiner Regina M. DeBerry	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Status of Application, Amendments and/or Claims

The references in the information disclosure statement, filed 20 November 2000 (Paper No. 4), have not been located. Regretfully, the references listed cannot be considered at this time. Applicants are invited to cite a particular reference(s) that they want to be considered. The information disclosure statements filed 10 October 2001 (Paper No. 6) and 05 March 2002 (Paper No. 11) were received and comply with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

The amendment filed 05 March 2002 (Paper No. 12) has been entered in full. Claims 1-27 were cancelled. Claims 28-34 are under examination. Applicant's election of species recombinant human erythropoietin in Paper No. 12 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The disclosure is objected to because of the following informalities: In the Brief Description of the Figures "FIG. 3A-B" should read "FIG. 3A-C" (page 7, line 9). Appropriate correction is required.

Claim Objections

Claim 33 is objected to because of the following informalities: Claim 33 encompasses a non-elected invention and requires amendment to limit to elected invention. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 32 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 32 is drawn to the method wherein said erythropoietin is administered at a dosage of 50,000 to 100,000 Units per administration or per day.

The instant claim lacks enablement because prior art teaches away from the instant dosages. Sakanaka *et al.* (Proc. Natl. Acad. Sci. USA Vol. 95 4635-4640, 1998) report that EPO, *in vivo* protects neurons against ischemia-induced cell death. Infusion of EPO into the lateral ventricles of gerbils prevented ischemia-induced learning disability and rescued hippocampal CA1 neurons from lethal ischemic damage (page 4637, results 1st-3rd paragraph and Figures 1-2). One unit of recombinant human EPO approximately

corresponds to 10ng of EPO protein. EPO at a dose of 0.5, 2.5, 5, or 25 units/day was infused for 7 days into the left lateral ventricle of each gerbil (page 4635, material and methods). Sakanaka teaches that EPO at a dose of 50 units/day or 500 units/day was ineffective in preventing the ischemia-induced reduction or response latency and neuronal loss (page 4637, 2nd paragraph and page 4638, 2nd paragraph). Sakanaka suggests that the hippocampal neurons with EPOR respond to EPO within a limited concentration range *in vivo* and that high concentrations of EPO induce a rapid down-regulation of EPOR, failing to transmit EPO-mediated signals to the neurons (page 4638, 2nd paragraph-4639). A similar experiment using rats was disclosed in example 4 of the instant specification (page 32, line 16-page 33, line 14). The concentration of EPO used for this particular experiment, however, was not disclosed.

Therefore in view of the contradictory state of the prior art teaching away from the instant concentrations of erythropoietin employed in methods for treating cerebral ischemia in mammals, claim 32 as cited is not enabled.

Claim Rejections - 35 USC § 102

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application

being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 28-31, 33 and 34 are rejected under 35 U.S.C. 102(e) as being anticipated by Sadamoto *et al.* (Biochemical and Biophysical Research Communications Dec. 9, 1998). The instant claims are generally drawn to a method of treating cerebral ischemia in a mammal comprising administering erythropoietin peripherally to said mammal. Sadamoto teaches ischemia models using rats. This is the same animal model used in the instant specification. Stroke-prone spontaneously hypertensive (SH-SP) rats with permanent occlusion of the middle cerebral artery (MCA) above the rhinal fissure and distal to the striate branches show a reproducible cortical infarct, place-navigation disability and secondary thalamic degeneration centered on the ventro-posterior nucleus. Sadamoto teaches that this rat model has an advantage over the gerbil model; it more closely mimics human patients with cerebrocortical infarction than does the gerbil ischemic model, and ischemia-induced behavioral abnormalities are easier to investigate in rats than gerbils (page 26, 3rd paragraph). Sadamoto states, "we now report the neuroprotective effect of EPO infused into the cerebral ventricle on place navigation disability, cortical infarction and secondary thalamic degeneration of MCA-occluded SH-SP rats" (page 26, 3rd paragraph-page 27).

After MCA occlusion, an osmotic pump filled with recombinant human EPO was implanted subcutaneously into the back of each animal and a needle from the minipump

was placed in the left lateral ventricle. EPO in a dose of 0.2, 1 or 5 U/day was continuously infused through the minipump for 28 days (page 27, 1st- 3rd paragraph). The left-to-right (L/R) ratio of cerebrocortical area in EPO-infused ischemic rats was larger than that of the vehicle-infused ischemic rats. Measurements of the L/R ratio of thalamic area indicated that EPO in the doses of 1 and 5 U/day significantly prevented the secondary thalamic degeneration in MCA rats (page 29-30 and Figure 2A). MCA occlusion in SH-SP rats caused the secondary degeneration of thalamic neurons and EPO infusion rescued the neurons (page 31, 2nd paragraph). Thus Sadamoto *et al.* anticipate the instant claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on Mondays-Fridays 8:00 a.m. - 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD
May 3, 2002

GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600